American Journal of Pharmacy

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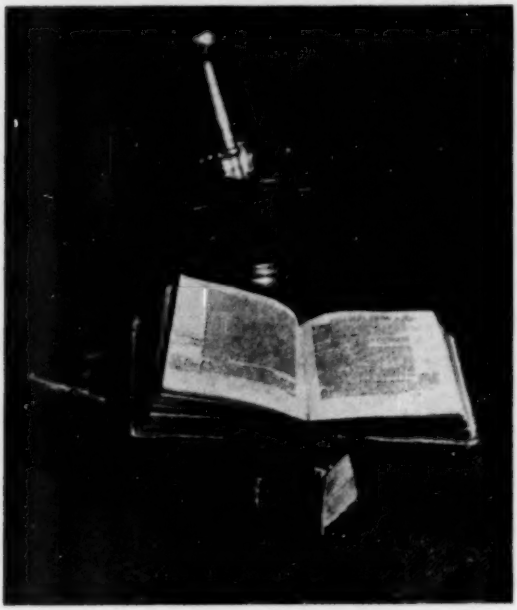

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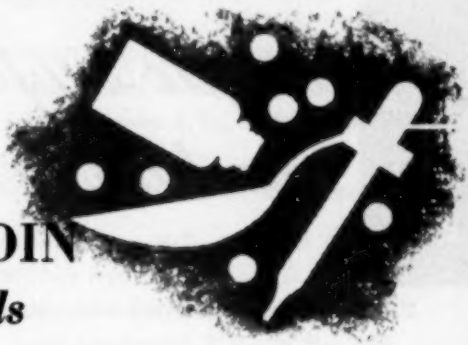

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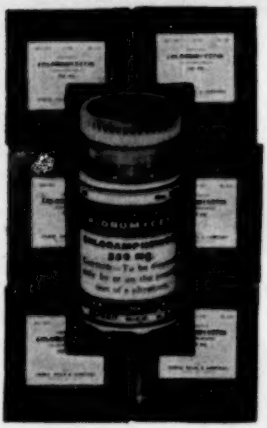

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AND THE SCIENCES SUPPORTING PUBLIC HEALTH

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EDITORIAL

A. PH. A.—N. A. R. D. CONTROVERSY

THE heated disagreement which has arisen over the course of action that should be taken on the prescription refill problem is ample evidence of a division in pharmacy which is both unfortunate and tragic. The A. Ph. A. has approached the problem on the premise that the Federal Security Administrator, who is the overall executive of the Food and Drug Administration, should grant a hearing so that some clarification of the stand taken by the F. D. A. might be obtained. Having a clear cut ruling, action might then be taken, if necessary, to protect the professional prerogatives of pharmacy. The N. A. R. D. is seeking legislative action through the proposed Durham-Humphrey Amendment to the Food and Drug Act. This amendment, presumably, would clarify the refill situation, although some important concessions would be made by pharmacy. Some of these are considered by the pharmaceutical industry as most objectionable, for example, giving the Food and Drug Administration the authority to decide which drugs may be sold on prescription only and which may not be sold at all by reason of their being either excessively dangerous or inert.

It is not our purpose at this time to discuss the refill problem itself. We have done this before and found our opinion shared by almost no one. It seems to us that a problem of even greater importance has developed as a result of the two great organizations of American Pharmacy working at cross purposes and without coordination and mutual support. Where, indeed, is the "united front" for pharmacy about which we heard so much a few years back? When was the last joint meeting held of the Council of the A. Ph. A. and the Executive Committee of the N. A. R. D.? What has happened to the joint resolutions which we once had setting forth a coordinated program for pharmacy in the United States? These are questions which demand an answer and the rank and file of American pharmacy must make this demand heard.

Little will be gained and much damage done as long as one organization attempts to justify its departure from cooperation and coordination by questioning the motivation of the other and suggesting that it does not have the true interests of pharmacists at heart. Such vilification is not only unjustified but it is in very poor taste and a discredit to all, accuser as well as accused.

Whether certain individuals like others or not is unimportant, the fact remains that as long as the two organizations are at loggerheads, each fencing for a more favorable position and trying to justify its actions with its members, nothing concrete of value to pharmacy can be accomplished.

The A. Ph. A. has done and is doing a splendid job in behalf of American pharmacy. The N. A. R. D. has rendered invaluable service in improving the economic status of the retail pharmacist. Each organization serves a certain distinct area of pharmacy but there are areas of activity and interest which must perforce overlap. It is here that close cooperation and joint action must be taken if the broad interests of pharmacy are to be protected and improved.

In pharmacy, as in the present world conflict, all differences could be settled if just a few key men would swallow a little pride, sit down amicably and each make a few concessions. Without such action pharmacy, just as the world, must see many of its "small people" hurt and injured paying a terrible price for the love of power by their leaders.

If in truth those to whom this message is directed love pharmacy and its practitioners why not show it in the manner best calculated to serve their interests? The truly great find it possible to forgive and forget. Small men in high places find it impossible.

L. F. Tice

CORRECTION

Volume 122, September 1950, p. 337. The lactone group in the structural formula given should be attached to carbon 17 rather than carbon 16 as shown.

CURRENT TRENDS IN MODERN MEDICINALS

Part II

By Madeline O. Holand D. Sc.*

DIAGNOSTIC AIDS

Bromkontrast

A brominated refined fatty oil, acid-free and free of bromine and bromide ions, is being tested as a contrast medium in bronchography. In 21 cases it was found to be highly satisfactory. Within 10 minutes after the procedure the medium was completely coughed up. It does not activate tuberculous processes.

It is prepared in two viscosities dependent upon the oil content. The viscous product is adjusted so that it does not enter the finer bronchi. It contains 45 per cent Br. If the clinical and x-ray findings do not agree with the bronchograph another one must be made using the nonviscous product. Only 20 cc. should be used so that not all the bronchial stems are filled. Some patients may be too weak to cough up the medium and would smother if too much was used. The nonviscous preparation contains 20 per cent Br. and also is indicated for fistula filling and sialography. The product known as Bromkontrast is stable for a maximum of 3 months.

Skin Test for Mumps

A skin test for mumps has been devised based upon a tuberculin-like reaction following the intradermal injection of an antigen composed of a formalin-killed egg grown virus partially purified by centrifugation. Florman, Fischer, and Moloshok reported before the Clinical Research Meeting at the New York Academy of Medicine the results of a study involving 135 skin tests of this antigen. Among the 135 individuals tested 26 were first cases of mumps and the rest were contacts. Among these contacts 80 were adults and 29 were children.

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* Editor, American Professional Pharmacist; Technical Editor: Medical Times, El Farmaceutico and Pharmacy International.

All of the first cases gave negative reactions during the illness but several months later 5 of 6 retested gave clearly positive tests and 1 questionably positive. Among the contacts 60 were found to give positive tests and 49 negative tests. Within 3 weeks 12 of the contacts became ill with clinical mumps. Of these 12 only one was a previously positive reactor while 10 of the other 11 previously negative reactors were children.

The conclusion has been reached, however, that although the test is useful in predicting susceptibility to mumps a positive skin reaction is not conclusive evidence of resistance to the disease.

Urokon

Recently a new iodine compound was reported to have certain advantages over the existing preparations as a diagnostic aid for excretory and retrograde urography. It is not only less toxic but also provides greater opacity to x-rays. Chemically this new compound is sodium-3-acetylamino-2,4,6-triiodobenzoate ($C_9H_5NO_3I_3Na$). The generic name is sodium acetrizoate. It has a molecular weight of 578.9 and contains 65.8 per cent of iodine. Occurring as a white, crystalline powder it is freely soluble in water.

The first clinical trials of sodium acetrizoate revealed that it caused few side reactions. The first tests were made with a 50 per cent solution but it was shown that a 30 per cent solution produced less side reactions without changing the quality of the urograms. Further studies were then made with the weaker solution in doses of 25 ml. Comparative tests with two other available media revealed that side reactions from sodium acetrizoate occurred in but 19 per cent of the patients. The other two media caused reactions in 62 and 36 per cent respectively. The side reactions observed included nausea, vomiting, arm pain, foreign taste, mild urticaria, severe urticaria, flush, dizziness and sneezing. The greatest reduction in reactions by the new medium was observed in the foreign taste, arm pain and nausea groups. No delayed reactions were observed in any patients inclusive of those with impaired renal function.

Tests of the quality of the pyelograms made with sodium acetrizoate have shown them to be consistently good.

Although this medium is given over a period of 4 minutes it appears in the kidney earlier and disappears more rapidly than another medium used as a comparison.

Sodium acetrizoate is believed to be better tolerated for retrograde use than is sodium o-iodohippurate dihydrate.

The usual toxicity tests showed that no toxic symptoms developed even when 4 to 8 times the quantity per Kg. of body weight necessary to x-ray the kidneys was given. Rats given 0.2 Gm. per Kg. of body weight for 2 weeks showed no microscopic changes in their kidneys.

Mallinckrodt Chemical Works is marketing this new agent as Urokon.

DRUGS USED FOR EFFECTS ON HIGHER NERVE CENTERS

Ether

MacCurdy of the New York State Psychiatric Institute has announced a new treatment for certain types of mental illness. It involves the use of ether administered intravenously. This therapy compares favorably with electric shock treatment and has certain advantages as follows: (a) Ether therapy may be applied to patients with physical conditions which prevent the use of electric shock therapy; (b) because there are no convulsive seizures, there is no danger of fractures or dislocations; (c) there is no evidence of anxiety when ether treatment is given as compared with patients undergoing electric shock treatments; (d) the patient has a sense of well-being and is in good contact with the physician at all times; (e) no unpleasant after effects, no confusion or disturbance of memory are experienced.

Ether has been used in treating mental ills before but it was given by inhalation and was only temporary in effect. In this new therapy it is injected slowly intravenously using a technic similar to that used for blood transfusions. Each treatment lasts from two and a half to three hours and is administered daily for from ten to twenty-seven days dependent upon the patient's requirements. After each treatment the patients experience a slightly elated feeling.

Thus far this therapy has been effective in affective or emotional psychoses and psychoses with depressive features.

Somnoform

A dental anesthetic composed of a mixture of ethyl chloride, methyl chloride and ethyl bromide, has now been found to be of

value as a "truth drug." It affects the nervous system in such a manner that inhibitions are released and the patient talks freely about the memories which have been suppressed and have caused mental disturbance. This combination of drugs is believed to be the closest to the ideal "truth drug." It is easy to administer by inhalation, does not excite or induce nausea and vomiting and can be administered over an adequate period without bad effects. The patient is completely under for about two minutes following which he can be interviewed for five to ten minutes. If necessary this can be extended to half an hour by another administration.

Known as somnoform this drug is marketed by Stratford-Cookson Company.

DRUGS USED IN THE TREATMENT OF CANCER AND LEUKEMIA

ACTH and Cortisone

Both ACTH and cortisone have been shown to bring relief in acute leukemia. However, they do not effect cures. It is believed that their value will be in the search for the cause of this disease rather than in the cure. However, this knowledge eventually may lead to the cure. Remission of some symptoms has been accomplished for approximately three weeks to two months. Second remissions were brought about in four patients. In eleven of the thirty cases there appears to be some prolongation of life.

In children, ACTH has been responsible for alleviating all of the desperate symptoms after a few days' administration. Further work is necessary on this subject.

Guanazole

A new cancer growth inhibitor, 5-amino-7-hydroxy-1-γ-triazole[d]-pyrimidine is being given intravenously in doses of 200 mg. daily. The intravenous solution is made up by adding an equimolar quantity of sodium hydroxide to 5-amino-7-hydroxy-1-γ-triazole[d]-pyrimidine. The latter is then made up in concentration of 5 mg. per cc. in physiological saline solution. This new drug is also being tested for its effectiveness orally given in capsules. Under the name Guanazole it is under investigation by Lederle Laboratories Division, American Cyanamid Co.

Testosterone and Thyroxin

Testosterone has been used effectively in treating breast cancer in women. However, it does produce masculinizing effects. These effects have been offset somewhat by the simultaneous administration of thyroxin according to Loeser. In addition the use of the two hormones also has shown good results in a few cases of cancer of the ovaries and of the uterus.

Either the female or male sex hormone alone tends to produce a deficiency of thyroid hormone thus disturbing the general body health. Consequently, use of the thyroxin offsets this effect.

IMMUNIZING AGENTS

Mumps Vaccine

Prior to the past year there was no vaccine available for the prevention of mumps. One has now been developed and is designed primarily for the immunization of large groups of children or adults, housed together in close quarters, as in schools, camps, institutions, or military installations, where a mass outbreak of mumps would cause serious inconvenience. It is, therefore, not recommended for routine use in the prevention of mumps in childhood, inasmuch as it confers immunity for only about one year and annual revaccination is necessary. Because mumps in adults is a serious disease it may be advisable also to administer the vaccine to susceptible doctors, nurses, college students, military personnel, etc. Lederle Laboratories Division, American Cyanamid Company, and Eli Lilly and Co., Inc. are marketing this new Mumps Vaccine under license by the National Institutes of Health where it was developed.

INSECTICIDES, RODENTICIDES

Warfarin Compound 42

Recently released by the U. S. Department of Agriculture for sale to the public is the amazing new killer of both rats and mice which was developed by the University of Wisconsin Alumni Research Foundation. This substance is related chemically to the anticoagulant, dicoumarol. It is used by mixing with any dry food stuff known to attract rodents such as oats, grain, dry cereal or dog

food. The pests are poisoned slowly yet continue to eat the bait until dead of internal hemorrhaging.

Warfarin Compound 42 is marketed by J. T. Eaton and Co., Inc. Warfarin is also an ingredient of Rax distributed by the Insecticide Division of Prentiss Drug & Chemical Co., of Ratrid by Vineland Poultry Laboratories and of Black Leaf by Tobacco-By-Products & Chemical Corp. and Dethmor supplied by S. B. Penick & Co.

NEW EQUIPMENT

Electrohysterograph

A new electrical apparatus can now be used to reduce the risks of childbirth. Developed by Steer at the College of Physicians and Surgeons, Columbia University, the machine will make it possible for the physician to determine whether labor is going to be normal or abnormal and whether the pains are positive labor pains. More than 200 patients have been tested thus far. Known as an electrohysterograph the apparatus records the electrical activity of the uterus as it contracts during labor. Six wires are fastened in pairs to the outer abdominal wall and they transmit the impulses to electrically-activated pens which write on chemically sensitive paper. The machine can be used right at the bedside. It is modelled after the electro-encephalograph. The electrical patterns produced during normal labor differ considerably from those produced by abnormal labor. Thus the obstetrician can make advance preparations.

As the uterus contracts it produces electrical activity which can be picked up by electrodes on various parts of the body.

Sterilizing Jar Lid

Hospital pharmacists are frequently confronted with the difficulty of keeping outside surfaces of ampuls sterile when submerged in sterilizing fluid contained in a jar. Ampuls containing powders, such as some spinal medications, are difficult to submerge resulting in the necessity of placing pads or sponges to weight and keep the entire ampul below the sterilizing liquid surface. Because this method is cumbersome contamination may occur during emergencies as well as considerable delay.

In the *Journal of the American Medical Association* recently there was described an improved lid for sterilizing jars. This lid provides for better contact with sterilizing fluid. It is a time-saver for personnel and simple to construct.

It consists of an ordinary sterilizing jar cover with a perforated disk on a post soldered or welded to it. The disk is made of ⅛ or 1/6 inch (0.32 to 0.42 cm.) stainless steel, and the post is a solid stainless steel bar ¼ inch (1.90 cm.) in diameter. This assures enough weight in the lid to submerge ampuls. To facilitate removal of the lid, holes are drilled in the disk allowing the sterilizing fluid to pass through. When the lid is removed, the ampuls automatically come out of solution and are easily handled. There is no searching under cotton or gauze for the ampuls. With replacement of the lid, the ampuls are automatically submerged ready for use again.

NEW TECHNICS

Atherosclerosis and Cholesterol

It was learned some time ago that there is a relationship between an excess concentration of cholesterol in the blood and the formation of the ulcers in the arteries which are responsible for hypertension and coronary thrombosis. A study of these ulcers revealed that the base contains an excess of cholesterol, phospholipids and fatty acids.

Hypercholesteremia is commonly associated with atherosclerosis, diabetes mellitus, nephrosis and myxedema. Because of this association further studies were conducted. It was found that these small ulcers often caused death in adults between thirty and forty years of age so that it was not necessarily a development of old age. However, further study showed, too, that some individuals have a high concentration of cholesterol in their blood but still do not develop any coronary disease. Investigation was then directed toward determining whether the structure of the molecule might be responsible.

Animal studies revealed molecules of varying sizes and the larger ones carried more cholesterol. Tests on humans revealed that their blood, too, contained both small and large cholesterol-containing molecules. Small molecules of 3 to 8 Svedberg units contained 25 per cent protein in addition to some cholesterol whereas the S.10 to 20 class contained 30 per cent cholesterol and little or no

protein. It is the S. 10 to S. 20 molecules that are always found in patients with atherosclerosis or in patients who are most likely to develop the condition.

In tests run on more than 700 patients it was found that these molecules were rarely present in the blood of normal women under forty, but were in one-third of the men of the same age level. This confirms the fact that young women are less likely to have this disease than are young men. The increase in frequency and severity of atherosclerosis above the age of forty was shown by the fact that fifty per cent of men and women had the larger molecules in their blood. Atherosclerosis is a serious complication in diabetes and a high percentage of this group also showed the presence of the larger molecules. In one hundred four men and women with coronary thrombosis ninety seven per cent also showed concentrations of the larger molecules in the blood.

The number of these larger molecules can be reduced in the blood by decreasing the quantity of fat in the diet. If this is continued they may even disappear within two weeks to a month's time.

The quantity of cholesterol in the blood does not necessarily indicate the presence of the larger molecules. There may be just as many in the blood of a person with a low cholesterol level.

This discovery is considered to be of value in diagnosing of impending atherosclerosis before the characteristic symptoms develop and also for predicting the susceptibility of the individual.

Automatic Administration of Anesthesia

A new machine has been developed by Bickford at the Mayo Clinic, which allows the patient to automatically administer his own anaesthesia during surgery. Called a servo-anesthetizer it is an electronic device which connects an individual's brain waves to a pump which sends a fixed amount of anesthetic agent into a vein or an ether vaporizer. Nicknamed "The Brain" this machine will not eliminate the need for the anesthetist and other technicians for it will still be necessary to supervise the administration of the anesthesia. However, he will be relieved of some of the tedious work and he will be aided in maintaining the patient at a more constant level of anesthesia. The new machine shows the change in depth of anesthesia several seconds before the usual visible signs on the patient. The ad-

ministration of the drug is automatically and instantly adjusted to compensate for the change.

Small wires with sharpened ends bent to form hooks are fastened painlessly to the scalp of the patient. They carry the output of the brain waves to the machine. The energy output of the brain waves decreases as the anesthesia deepens and as this occurs it activates a relay system which controls the injection of the anesthetic agent into the vein or ether vaporizer. The brain waves can be viewed continuously on a small screen in front of the machine, or can be inscribed on paper tape for permanent recording. The patient is prepared in the usual manner and then the machine is brought into use.

Blood Preservation

One of the great difficulties in handling blood for use therapeutically has been the preservation of the various components. As soon as blood is withdrawn from the body deterioration begins. Glass flasks and rubber tubing are destructive to certain elements and, in particular, the white cells. The calcium in the blood is responsible for speeding coagulation. For this reason citrate was added to prevent coagulation. However, citrate does destroy some blood components.

Recently Cohn at the Harvard Medical School demonstrated new apparatus and technics for collecting and preserving blood and for separating it into its fractions. A plastic receptacle has been designed which has a narrow neck filled with resins which remove the calcium from the blood as the blood flows into the container. A plastic tube of the same material as the receptacle is used to draw the blood through. This plastic tubing also will be used in direct transfusions making them more beneficial since it is believed that the rubber tubing now used affects the blood so that it is not completely viable as it is transfused.

New apparatus and technics also have been developed for separating the many components and several new components have been separated.

Blood Tests

A flame electro-photometer has been developed by Brown of Hahnemann Medical College which determines the concentration of potassium and sodium in a specimen of blood serum in five minutes

as compared to twenty-four hours by the methods now used. The flame is composed of propane gas and oxygen. As a small container of blood serum is placed near it the flame becomes brilliant depending upon the concentration of sodium and potassium. The delicate electric meters record the brilliance and measure the chemical content. A group of standard specimens are used for comparison to determine the exact quantities. Use of this apparatus will be invaluable in the diagnosis of shock, heart disease with kidney involvement, meningitis and malignant hypertension with uremia. It will enable the physician to make the diagnosis much more rapidly. The apparatus is also being used for research into heart diseases and for determining the water balance between the tissues and the blood stream.

Blood Typing

A faster, easier and more accurate blood typing system has been developed by Taylor recently. In addition, it requires less clerical work and can be readily taught to others. The individual to be tested is given a card on which he fills out his name. Three smears of his blood are then made on the card and 3 serums are applied to each. The red and blue dyes are used to match type A, B, AB or O and the colorless dye is for determining whether the Rh factor is positive or negative. When the blood is dry on the card the card can then be filed as a permanent record. The patient is given a card with the necessary information on it for his records. This technic has been tested on 2000 people without an error.

Diagnosis of Fungus Infections

At times, various fungus infections prove difficult to diagnose. Recently the University of Pennsylvania Medical School reported the discovery of a simple and accurate diagnostic technic for the many known varieties of fungi. Cellulose is present in most plant structures and cells and since fungi are plants they contain cellulose. Human beings are considered in the animal class and animal tissues do not contain cellulose. Therefore, the discoverers of this diagnostic technic reasoned that a dye which colors cellulose might be useful in the differentiation.

Thus it was discovered that fuchsin of the Hotchkiss-McManus stain when applied to the infected areas dyed the cellulose-containing

fungus cells a deep magenta and did not affect the surrounding tissues. After the discovery the technic was tested in an epidemic of tinea capitis. Microscopic examination of the hairs in the follicles of afflicted patients showed that they were surrounded with a necklace-like formation of garnet globules after the basic fuchsin was applied.

The deep-seated fungus infections which are so often diagnosed as malignancies because of the x-ray picture are differentiated by applying the basic fuchsin to biopsy specimens, sputum, urine, lymph and other effluvia from afflicted areas.

Epileptic Mice

By inbreeding mice for more than 50 generations at the Roscoe B. Jackson Memorial Laboratory of Bar Harbor, Maine, a strain has been produced which goes into convulsions when a doorbell is rung. These mice will be used to test the effectiveness and dosage of drugs with possible value in treating epilepsy and other brain and nervous system conditions. Seventy-five per cent of the males and 65 per cent of the females die of convulsions when the bell is rung.

Frozen Sleep

Surgical repair of dogs hearts has been accomplished by the use of frozen sleep to stop the heart temporarily. When the temperature of the body drops just below 90 degrees Fahrenheit unconsciousness occurs. All reactions are slowed down. The heart beats more slowly and the need for a rapid supply of oxygen decreases and the slower rate keeps the individual alive. No bad effects have been observed in persons kept unconscious in this manner for several days.

As a result of experiments on dogs it is believed that this can be used on humans when surgery on the heart is necessary. Frozen sleep would allow more time than is now allowed by ordinary anesthetics.

Gallstones

High-frequency sound waves have been effective in breaking up gallstones in rabbits and dogs. By means of an abdominal incision the ultra-sound was introduced directly on the gallstones without damaging the surrounding tissues. The gallstones were broken into small pieces which then passed into the intestines and were excreted. Human gallstones were tested by placing them in loops of rabbit

intestines brought outside the body. About eighty per cent of the stones were broken by a burst of ultra-sound. Live tissue can be protected by transmitting the sound through water. The tissue is as elastic as the water and stretches without tearing.

Invert Sugar

Weinstein, at a meeting of the American Therapeutic Society, reported on a technic for more rapid intravenous feeding of carbohydrates to patients who are unable to take nourishment orally. In the past dextrose has been given intravenously to supply the carbohydrate necessary but in order to supply enough calories it must be given all day. Using invert sugar, Weinstein has found that he can give 100 Gm. in 56 minutes and 98.4 to 99.4 per cent of the sugar is assimilated. Four hundred calories are supplied by 100 grams so that in a relatively short time sufficient calories can be administered. Such feeding is generally needed in the first 3 to 5 days after an operation. However, it is also helpful in building up the reserve of patients who have been ill for a long time before an operation. Further studies on the use of invert sugar are being conducted. More promising results have been obtained by mixing proteins and the invert sugar so that only one intravenous treatment is required.

Insecticides

So many liquid or powder insecticides even though sprayed are not efficient because the underside of the foliage is not covered. Smooth stems also are resistant to sprays. Yadoff, a French scientist, has developed a method of overcoming this. The insecticide is electrified by blowing the powder at supersonic speed through a fine nozzle. The apparatus used has been patented. It consists of a horizontal steel bottle and an air compressor. A narrow tube runs through the steel bottle and is connected at one end with the nozzle and at the other with the insecticide. The compressor fills the bottle under pressure. By means of a valve the air is admitted to the nozzle and takes with it the insecticide. The friction of the air at supersonic speed and the slow-moving insecticide particles generates the electricity. Thus the particles are electrified and as they emerge in a fine mist the entire plant is covered and the particles cling as only electrified particles can.

Kidney Stones

Vermeulen, Goetz, Grove and Ragins have reported 3 ways of dissolving kidney stones in rats. It is hoped that at least one of the 3 methods can be applied to kidney stones in human beings thus eliminating pain and surgery.

Kidney stones are composed of calcium, magnesium and other chemicals which form hard deposits in the kidneys. In the test animals stones were produced by placing tiny flat pieces of zinc in the rats' bladders to serve as seeds for the growth. One method employed to dissolve the stones was to increase by 4 times the urine output. This was accomplished by giving the rats great amounts of sugared water daily for six weeks. Stones did not develop in rats placed on this regime immediately and in those which already had stones they were dissolved. By letting the stones develop, removing and weighing them and then replacing them in the rats before allowing them to drink lots of liquid this latter fact was discovered. The same effects were achieved by adding ammonium chloride to the food thus making the urine more acid. Similar results also were obtained by decreasing the amount of magnesium in the rats' food.

Another interesting but puzzling fact was uncovered in the experiments as well. When a radioactive substance was placed in the bladder no stones formed whereas the same substance without radioactivity produced stones. Further investigations are being made on this subject.

New Instrument for Treating Cancer

Shimkin, of the San Francisco laboratory, sponsored by the University of California and the National Cancer Institute, has developed an instrument which shoots anti-cancer drugs with almost pinpoint accuracy into deeply buried malignancies. A ribbon-like tube or catheter with a nozzle on one end is inserted at a convenient place in the artery and pushed further until the nozzle reaches a secondary artery supplying blood to the cancerous area. The plunger on the outer end of the tube is then used to force the drug into the artery where the blood stream carries it directly to the cancerous area. Because most drugs which destroy cancer cells also destroy normal cells this method may allow for the use of higher concentrations of drug. The apparatus, however, is still in the experimental stage.

Sterilizer

Sterilization of vaccines, serums and other pharmaceuticals can now be accomplished by means of high-voltage cathode rays after they have been placed in containers and packages. An electrostatic generator at M. I. T. produces 3,000,000 volt cathode rays which sterilizes such substances as penicillin, streptomycin, surgical sutures and anticoagulants, after they are sealed in glass containers. There are no detectable effects on potency or other properties. In the sterilization process the temperature is raised less than eight degrees.

Ultra-Violet Sterilization

It has been common knowledge for some years that certain cells and micro-organisms may again live after they have been killed by ultraviolet light or x-rays. However, in more recent studies it has been shown that ordinary light restores such killed organisms to life. The theory has been advanced that the ultraviolet light alters some constituent in the cell, thus killing it and that visible or ordinary light restores this constituent to the original condition. Experiments with x-ray killed organisms revealed the same effects. A mixture of ultraviolet and ordinary rays reduced the killing power of the former. It also reduced the frequency of mutation of the organisms as caused by ultraviolet radiation.

PEPTIC ULCER

Banthine

The etiology of peptic ulcer is unknown but various theories have been advanced such as hypermotility, hyperacidity, various peptic enzymes, end-artery thrombosis or spasm, body type, allergy, focal infection and psychic trauma. In some cases of peptic ulcer it may not be possible to prove that any one of these is responsible whereas in others there may be several factors present. The single factor most commonly accepted as responsible for development of the ulcer has been gastric acidity. However, now it is believed that gastro-intestinal hyperirritability and hypermotility may be just as important. In reviewing the various substances used to reduce acidity it was found that they might have more influence on motility than on acidity.

Recently, the discovery of a new drug, β-diethylaminoethyl xanthene-9-carboxylate methobromide was announced and it shows great promise in this new approach to ulcer therapy. It is a quaternary amine and dissolves readily in the commonly used solvents as well as in gastric and intestinal secretions. Belonging to the group of parasympathetic blocking agents this chemical, commonly known as methantheline bromide, acts particularly to depress the secretions of humans. However, it also has a more important effect in that the motility of the whole gastrointestinal tract is decreased after its administration.

Human studies of this new drug were directed chiefly toward the effects on the cardiovascular and gastrointestinal systems and for any untoward reactions.

In the studies on the cardiovascular system it was found that there was a moderate rise in the pulse rate as well as a slight rise in blood pressure following an oral dose of 100 mg. However, no marked changes were noted in any one patient and no postural hypotension occurred.

Studies of methantheline bromide for its effects on gastric motility by means of the intragastric balloon technic and by visualizing the traverse of a suspension of barium both fluoroscopically and roentgenographically showed that following intravenous injection the contraction waves stopped immediately (the rapidity and degree dependent upon the dosage). Following oral administration of 100 mg. the gastric contraction waves ceased or decreased in intensity less promptly but the effect lasted for a longer period of time. Forceful waves of contraction returned more gradually after oral administration than after intravenous administration. Fluoroscopic and roentgenographic studies revealed that peristalsis was either sluggish or absent and there was considerable delay in the emptying into the duodenum following administration of this drug. In gastric secretion studies it was found that there was a rise in pH, a decrease in free and total acid quantities and a decrease in the volume of gastric secretions.

The propulsive contractions in the small intestines almost completely stopped in 35-50 minutes after oral ingestion of 100 mg. and was maintained for about 4 hours.

Normal colonic activity was reduced within 15 minutes after oral administration of the drug and continued for over 2 hours. The

parasympathetic stimulating effect of beta-methylcholine chloride was controlled by administration of methantheline bromide. The gastrocolic reflex also was inhibited by administration of 100 mg. of the drug whereas no such effect was observed when 200 cc. of milk were given. An equivalent amount of atropine to produce similar effects would result in tachycardia, cycloplegia and excess dryness of the mouth.

Because methantheline bromide possesses these anticholinergic effects which counteract the vagotonia associated with peptic ulcer clinical studies were made. The results obtained in the first trials were very promising. Seventeen of the first 20 patients were considered to need surgery. However, when given 100 mg. of methantheline bromide orally or intramuscularly immediate improvement was observed. Within 15 minutes relief of pain occurred in a majority of the patients and did not recur if the patient was given 50-100 mg. doses orally every 5-6 hours day and night. Peristalsis in the stomach and intestines was decreased as was the volume of stomach secretions. The free acid content of the secretions was reduced or eliminated entirely. The ulcers healed over in all of the first 20 patients. Studies on additional patients confirmed these preliminary observations.

The recommended dosage of methantheline bromide is 50-100 mg. every 6 hours day and night. However, as with most drugs, the dosage should be adjusted according to the severity of the condition and to the patient.

Mouth dryness or blurred vision are often observed in patients particularly if they are taking therapeutic doses. Usually they are minor in nature and oftentimes disappear even though medication is continued. In some few cases they may be severe enough to indicate that the dose be reduced.

Methantheline bromide is available as Banthine from G. D. Searle and Co., Inc.

Chloresium Powder

Chlorophyll, through the past few years, has been used more and more widely. Now it has been shown to have value in treating peptic ulcers. Prepared in powder form there are, along with the water-soluble derivatives of chlorophyll, the antacids aluminum hydroxide and magnesium trisilicate. The base is dehydrated powdered okra.

This product is designed to bring to the treatment of peptic ulcers the tissue-stimulating properties of water-soluble chlorophyll. The specially prepared okra base provides a tenacious coating material which performs the essential function of holding the chlorophyll in prolonged contact with the ulcer crater. The addition of aluminum hydroxide and magnesium trisilicate provides prompt antacid action without danger of alkalosis or interference with bowel regularity. Clinical trials have shown this product to be effective in chronic ulcer cases which had resisted previous therapy. Good results were achieved without the usual restrictions on diet, smoking, alcoholic beverages or general activity. The average dosage of this preparation is 1.8 Gm. 5 times daily (upon arising and retiring and after each meal). A small amount of water may be used to aid in swallowing the powder. Fluids or solids taken within one and one-half hours after taking the powder lessen its effect and should be avoided whenever practicable.

This product, known as Chloresium Powder, is marketed by Rystan Company, Inc.

Hexamethonium Iodide

Hexamethonium iodide, the hexa derivative of polymethylene-bistrimethyl-ammonium series of compounds, has been found to have a potent effect on gastric secretion and motility. The compound was administered intramuscularly in doses of 100 mg. A single 100 mg. dose of hexamethonium iodide (C6) produced achlorhydria for as long as 3 hours and repeated doses effect a substantial reduction in the volume and acidity of the night secretion. The compound also prevents the development of a true insulin response, fails to prevent a histamine response, and produces a prolonged inhibition of gastric motility. The high potency of hexamethonium iodide and its comparative freedom from side effects suggests the use of this compound in the treatment of peptic ulcer.

POLIOMYELITIS

Food Allergy

Studies of a number of poliomyelitis victims who have been crippled have revealed that allergic sensitivity to certain foods may make the individual more susceptible to poliomyelitis, particularly the

crippling type. It is believed that active allergies may predispose a person to poliomyelitis because the resistance is lowered. Of 249 poliomyelitis victims all were found to have signs of 2 or more allergies whereas of 246 students free from poliomyelitis 33 per cent had either no signs of allergies or signs of only one allergy. The remainder of the students without poliomyelitis did report symptoms of 2 or more allergies. Another study in a different locality reported similar results. The allergic signs included enuresis, constipation, abnormal tiredness, pulse beat over 84, inflammation of the nose membranes, neuralgia and headaches. In many instances these symptoms had been observed in the students just prior to the poliomyelitis attack.

Poliomyelitis Vaccine

A vaccine which has immunized 90 per cent of a group of experimental animals against one strain of poliomyelitis has been developed at the Michael Reese Hospital in Chicago. The vaccine was prepared by bombarding the polio virus with rays from a new type of ultraviolet lamp. The tests have been successful on mice and monkeys but considerable work must be done before the vaccine can be tested on humans. The animals were vaccinated with the protective substance and then the live poliomyelitis virus was injected into their brains. With mice the immunity achieved was 90 per cent and with monkeys 50 per cent. The aim, of course, is to develop a polyvalent vaccine which will immunize against the 3 types of poliomyelitis. Other laboratories have developed vaccines which have protected animals. However, it has been observed that the usual chemical methods, such as inactivation of the virus with formaldehyde, also destroys a greater portion of the activity of the protective substance in stimulating resistance.

RADIOACTIVE COMPOUNDS

Of the more than 700 radioactive tracer atoms which have been prepared only six are considered to be of importance at the present. These 6 are iodine, phosphorus, gold, sodium, manganese and arsenic.

Radiophosphorus is used in treating diseases of the blood and blood-forming tissues. Radioiodine is effective in the therapy of thyroid cancer and goiter and in determining hyperactivity of the thyroid. Recently it was found to be effective as well in relieving heart

pains, shortness of breath and fatigue. This new use was reported at a meeting of the American College of Physicians by Blumgart, Freedberg and Kurland of Beth Israel Hospital and Harvard Medical School. The radioactive iodine is administered in water. Twenty-two patients with either angina pectoris or congestive heart failure who were complete invalids were given the treatment. Four were able to return to work and many others reported that they could once more enjoy life at home. The radioactive iodine decreases the production of thyroxin in the body and thus the weakened heart does not have to work so hard. One-third of the patients derived no benefit.

Both radiophosphorus and radioarsenic have the property of moving into all parts of the body. As they do so they give off gamma rays producing a similar effect to x-rays. Similar effects are achieved by radiogold and radiomanganese but less is known about these two substances. Radiogold has been used to halt the growth of tumors by injecting it directly into the tissue.

Another development in radioactivity is the 2 gardens which are being cultivated at the University of Chicago and the Atomic Energy Commission's Argonne National Laboratory in Chicago. The plants are being treated with radioactive substances so that various phases can be studied such as certain medical situations in which the isotopes from the atomic piles cannot be used directly. Also they wish to determine the effects of radioactivity on the plants as well. Foxglove is being grown in sealed battery jars and given a diet of radioactive carbon dioxide. From the plant then is obtained radioactive digitalis glycosides which can be traced in the body by means of Geiger counters.

From radioactive alfalfa they are obtaining radioactive amino acids, sugar and proteins. These latter products are used to study the means by which humans consume energy-producing foods. By feeding such radioactive alfalfa to hogs they hope to make the animals radioactive and thus obtain radioactive insulin from the pancreas. Plans are under way for a radioactive barnyard since the animals may exhale harmful quantities of radioactive carbon dioxide.

Algae have been made radioactive as the first step in making fish radioactive since haddock may prove to be a better source of insulin than is the pig. In order to produce better oysters a trial crop is being fed radioactive foods in order to determine just what

oysters eat. Radioactive vitamins will sometime in the future lead in the tests to determine human food intake.

The opening of the atomic apothecary at Oak Ridge, Tennessee, is another advance in this field. This is a specially designed setup to facilitate faster, safer, more plentiful and less expensive processing of the radioactive compounds for use in medicine.

TOOTH DECAY

Sodium Monofluorophosphate

A new chemical, sodium monofluorophosphate, has been found more effective in preventing tooth decay than sodium fluoride. In tests with hamsters, the former compound did not cause mottling of the tooth enamel as sodium fluoride so often does. The sodium monofluorophosphate also was more easily picked up by the growing tooth.

VEHICLES

Polysorb

A new, hydrophilic absorption base consisting of sorbitan sesquioleate in a wax-petrolatum mixture recently has been made available. Known as Polysorb it is non-irritating to the skin and mucous membranes, of neutral pH and capable of absorbing 8 to 10 times its weight of water. Tests for compatibility have shown it to be compatible with the following compounds: acriflavine, aluminum acetate, ammoniated mercury, belladonna, peru balsam, beta-naphthol, boric acid, calamine, calomel, camphor, chlorobutanol, chrysarobin, coal tar, cod liver oil, epinephrine hydrochloride, ethyl aminobenzoate, gentian violet, glycerin, hydrogen peroxide, ichthammol, iodine, iodoform, lead subacetate, mercurial antiseptics (organic), penicillin, phenol, sulfurated potassa, salicylic acid, sulfathiazole, sulfadiazine, sulfamerazine, sulfur, tannic acid, undecylenic acid, urea peroxide, zinc oxide and zinc undecylenate.

This base and its hydrated mixture can be applied easily to both dry and moist skin and mucous membranes. Its wax content apparently removes much of the tackiness inherent in petrolatum. Physically the vehicle has a desirable sheen and is smooth, white and of good consistency. With warm water it is easy to remove the highly hydrated base. This base is particularly recommended for ophthalmic use because of the limitations of the alkaline o/w bases.

SCS

Sodium cellulose sulfate, a cellulose gum, is a light tan, dense, free flowing powder soluble both in hot and cold water. It is available at present for experimentation in medium and low viscosity grades. In a 1 per cent solution the pH is 6 to 8. The solutions are clear and viscous and are easily prepared if the dry powder is added slowly to the water with vigorous agitation. If available, a high speed mechanical stirrer is of value. The use of warm water results in more rapid solution.

As with similar substances the viscosity of the solution is increased with the concentration of the sodium cellulose sulfate and a gel may form at high concentrations. Viscosity also is influenced by temperature and it decreases as the temperature rises. This is usually temporary unless the exposure to temperatures above 75° C. is prolonged.

Sodium cellulose sulfate is very stable. The low viscosity type is especially so. Very strong, mineral acids may precipitate the medium viscosity type. However, precipitation seems to depend upon the nature of the acid rather than on the pH of the solution. Viscosity of the solution is somewhat decreased by acidification with the stronger acids. Boric, formic, acetic and citric acids cause no decrease at all.

If a strong alkali is added to a solution of sodium cellulose sulfate the viscosity is decreased immediately. At or above a pH of 11 it is decreased to 23 to 35 per cent of the original value. It is further decreased upon standing. Sodium cellulose sulfate is extremely resistant to hydrolysis.

Good compatibility with inorganic salts is shown by the medium viscosity type and excellent compatibility by the low viscosity type. The change in viscosity of the low viscosity type is only slight as the quantities of inorganic salt added are increased. However, with the medium type the viscosity rises sharply and, as the amount of salt is increased, reaches the precipitation point. When this point is reached the viscosity drops almost to that of water. Moderate quantities of water soluble organic solvents also are compatible with aqueous solutions of sodium cellulose sulfate. Here again, the low viscosity type is more tolerant than the medium type. Glycerin, ethylene glycol and propylene glycol are satisfactory plasticizers if a free film of sodium cellulose sulfate is desired. Solutions of sodium cellulose sulfate also

are compatible with gelatin and the well known water soluble gums. If desired they may be used together.

From the toxicity studies made thus far, sodium cellulose sulfate appears to be completely non-toxic. Preliminary results from long range feeding experiments also appear to be promising.

Sodium cellulose sulfate has the following non-pharmaceutical uses: as a detergent additive; as a film former and viscosity modifier in water and emulsion paints; as a stabilizing agent and thickening agent in certain food products; in the preparation of grease- and oil-proof papers; in the textile field; and in the packaging field. Pharmaceutically, this substance may be used in preparing water soluble lotions, creams, pastes and ointments. Water soluble capsules for administering various medicaments may be made from films of sodium cellulose sulfate. It also should prove useful in the cosmetic field for preparing greaseless creams and lotions, dentifrices, hair waving lotions and similar products.

Known as SCS sodium cellulose sulfate is being marketed by Tennessee Eastman Corporation.

VITAMINS

Although the subject of vitamins has been covered in previous reviews there are a few new concepts which should be considered here.

B-Complex

Horwitt, Lieberb, Kreisler and Wittman recently reported on the results of a five-year study of the human requirements of the B-complex vitamins. They believe that there is a relationship between the mind and these vitamins. Mentally infirm individuals appear to deteriorate when there is a deficiency of B-complex vitamins. However, they could find no evidence that adequate quantities had any value in treating mental disease. Although the aged appeared to require about the same quantity as did younger adults, the former did appear to be less resistant to the ill effects of low vitamin B diets.

New Mechanism of Vitamin Deprivation

Dietary inadequacy, faulty utilization, defective absorption, or faulty digestion of vitamin precursors are known to cause vitamin

deprivation. None of these mechanisms, however, can account for the selective deficiency of nicotinic acid, riboflavin, pyridoxine, and folic acid in sprue. This selectivity is in itself striking for these vitamins are all essential growth factors for bacteria. It has previously been shown that there are large numbers of bacteria within the absorbing areas of the small intestine. Frazer, therefore, suggests that in the sprue syndrome intestinal bacteria invade the upper small intestine from time to time in large numbers. These bacteria then compete with the host for common essential nutrients such as the B vitamins mentioned. In many cases the bacteria are the victors and the host shows signs of deprivation.

This competitive hypothesis would account for the peculiar selective deficiencies of sprue. The bacterial invasion may be related to fixation of pH as a result of achlorhydria and possibly to the presence of suitable food materials due to delayed absorption. The extremely high oral dosage required for vitamin therapy in these cases may also be explained in the fact that sufficient vitamin must be given for both the bacteria and the host.

The possibility also has been mentioned that bacterial competition in the intestines may be an important factor in other disease conditions wherein there are accompanying vitamin deficiencies. Particular attention was called to pernicious anemia in which vitamin B deficiencies are well recognized. The metabolic demands of a varying but essentially non-pathogenic bacterial flora in the intestine may be the key to the problem of the multiple but selective vitamin deficiencies in these and other disease conditions.

New Theory

Intestinal bacteria definitely play a role in producing essential nutrients according to recent reports. It has been found that by eliminating bacteria the resultant deficiencies can be checked. This can be accomplished by raising sterile animals or by killing the intestinal bacteria with sulfonamide drugs. Elvehjem and his colleagues have found that rats given a synthetic diet plus sulfonamide drugs lose weight because the growth vitamins and their manufacturers, the bacteria, were destroyed.

Next the number of bacteria and the vitamin concentrations which they contribute were determined. It was found that bacteria are responsible for a certain proportion of the vitamins since more vita-

mins were excreted than were administered. Different animals require various amounts of vitamins. The number of bacteria and their adaptation to the intestinal environment influences the vitamin supply in the intestines. In addition, if the concentration of folic acid is high that of biotin is low and vice versa. Even though animals were fed vitamin-deficient diets deficiencies of biotin and folic acid were hard to produce because the intestinal bacteria made these vitamins. Deficiencies of the older known vitamins were easier to produce because only small amounts of these are provided by the bacteria.

Sulfonamide drugs which decreased growth in rats stimulated growth in chickens. It is possible that the growth accelerator factor in aureomycin is thus explained. Since aureomycin and the sulfonamides destroy bacteria they may destroy those which are destructive to vitamins. As a consequence vitamins in the diet can be assimilated and growth occurs.

MISCELLANY

Antabuse

Tetraethylthiuram sulfide is the drug currently being studied for its value in treating alcoholism. One of the disadvantages of this compound is that when it is present in the body and an alcoholic product is consumed the individual suffers violent side reactions which are exceedingly dangerous. Jokivartio in Helsinki, Finland, recently reported that injections of an iron solution counteract this violent reaction. The solution known as Ferroscorbin consists of ascorbic acid and ferrous chloride in distilled water.

Basaljel

For the prophylaxis of the troublesome and resistant phosphatic stone occurring in kidneys, ureters and bladder a new form of alumina gel with high aluminum content and hence a high phosphorus-binding power has been made available. Clinical studies have shown that this product, in adequate dosage, and with regulation of phosphorus intake, diverts phosphate excretion to the intestine, virtually eliminating it from the urine. Thus it will check enlargement of phosphatic calculi already present, will prevent recurrence after removal, and will guard against renal stone formation in immobilized patients. Efficacious, even in the grossly infected urinary tract (when an acidifying regime

would be futile) and in the presence of kidney impairment, this therapy is also safe. There appears to be no danger of acidosis, kidney damage or unfavorable effects on metabolism. Wyeth, Inc., are marketing this product.

CF 9

In the past year a new drug was described in England as being effective against a fatal virus disease in dogs. It was thought that this drug also might have some effectiveness against the common cold. During the eighteen months of veterinary investigation, this drug was found to completely reverse the mortality figures for hard-pad (para distemper) so that instead of eight out of ten dogs dying, eight of ten now live. Veterinary surgeons believed this drug to be the most effective therapy yet found for this disease. CF 9 also has shown some effects on other virus infections in cats and dogs. Because it has a very low toxicity and negligible side effects, it is now being tested for its value in treating colds in humans. The Edenhall Clinical Research Center in London developed CF 9.

Chemical Fever

In the preparation of solutions for injection one of the most important factors is the removal of pyrogens and in most cases everyone considers these substances as of no value. However, recently a use for pyrogens has been reported. It has been found that artificial fever treatments are helpful in treating certain cases of malignant hypertension involving blindness, damaged kidneys and weak heart action. The artificial fever is produced by injecting pyrogens into the body. Only a moderate fever of 102 to 103 degrees Fahrenheit is produced. At present the theory advanced for this therapy is that the pyrogens are effective partly because they cause fever and partly because they stimulate the body's own resistant forces.

Chlorophyll As a Deodorant

Recently Westcott announced the discovery that water soluble fractions of chlorophyll are capable *in vitro* of neutralizing malodorous substances of neutral, acid, or basic reactions. *In vivo* tests revealed that the specially prepared chlorophyllins effectively neutralize obnoxious odors in the mouth from foods, beverages, tobacco, and

metabolic changes (halitosis). In addition the obnoxious odors from perspiration due to physical exercise, nervousness and illness; obnoxious foot odors, menstrual odors, and many urine odors from ingested materials, are also effectively neutralized. The dosage of the chlorophyllins as prepared in tablet form is one or two tablets daily at breakfast time. They may be swallowed with water or dissolved in the mouth. There are several products now marketed as follows: Odolex, Walker Vitamin Products, Inc.; Ennds by Pearson Pharmacal Co., Inc.; Nullo by The De Pree Co.; Chlorodon by Pitman-Moore, Inc. and Sudroma by Charles S. Frosst (Canada).

If the use of these chlorophyllins substantiates the reports from clinical trials the effect on established body deodorants may be revolutionary. The fractions used are completely free of toxicity.

Co-Salt

A new and different salt substitute which tastes like salt, looks like salt and sprinkles like salt has been developed. It contains choline, potassium chloride, ammonium chloride, and tri-calcium phosphate and is indicated for use as a salt substitute in salt (sodium)-free or restricted diets. It is designed to hold intake of edema-causing sodium to a minimum, secure maximum patient cooperation in diet maintenance, and thus to keep patients better nourished. Known as Co-Salt it is marketed by Casimir Funk Laboratories, Inc.

Common Denominator

Cancer, tuberculosis, rheumatic fever and rheumatoid arthritis, the four diseases most difficult to cure have been found to be linked by a common denominator according to Bonilla and Hess at the recent meeting of the American Chemical Society. The denominator is an abnormal amount of the simple sugar, fructose, found in the blood of patients suffering from any of the four diseases, which are among man's most crippling and lethal ailments. All four diseases are concerned with the complex carbohydrate-containing proteins known as mucoproteins which many years ago were found to occur in large amounts in the serum of cancer and tuberculosis patients. The test employed to determine the bound sugar involves diphenylamine. In the serum of diseased persons, the reagent produces a purple color of deeper intensity than in that of healthy persons.

DHE 45

Dihydroergotamine methanesulfonate has been found to control the pain in shingles (herpes zoster) in 75 per cent of the patients on whom it has been tried. Of the 40 patients 17 reported complete relief after each injection. Seven patients were given the drug intravenously and 10 intramuscularly. In most cases the pain was relieved in 15-20 minutes. In some the pain did not disappear completely but it was relieved. In 2 instances only 1 injection was necessary to provide complete and permanent relief. In others the period of relief varied from 8 hours to 3 days.

In most cases 3 to 4 injections were necessary. One required 5 and another 6. The drug did not appreciably alter the clinical course of the eruption. The patients who were listed in the group of failures included one patient with leukemia, one with advanced cancer of the lung, and four with post-shingles pain of protracted duration. However, some of these did report moderate temporary relief.

Certain side effects were experienced such as a temporary fall in blood pressure in 2 patients, moderate headache for a few hours in one and nausea and vomiting after each injection in another. Two patients experienced temporary bradycardia.

The dosage employed in most cases was 1 cc. but in some 2-3 cc. were given.

Dihydroergotamine methanesulfonate under the code name of DHE 45 is being investigated by Sandoz Pharmaceutical Division, Sandoz Chemical Works, Inc.

Diiodopropyl fluorophosphate

When tested on animals by the Army Chemical Center at Edgewood, Md., diiodopropyl fluorophosphate was found to inhibit temporarily the natural equilibrium center in the brain. As a result the animals walked in circles. The compound is injected into the carotid artery leading to the brain. The eye pupil on the side where the injection is made almost immediately becomes constricted. This is followed by the head turning in the opposite direction and the circling begins and continues for 2 to 3 hours. Even blindfolding of the monkeys did not stop the circling. Administration of atropine or scopolamine stops the circling immediately. If the drug is given in slightly larger dosage than that which causes the circling violent convulsions occur.

Dust-Seal

A new product marketed recently is claimed to aid those individuals who suffer from house dust allergies. Substances, technically known as house dust are inhaled by individuals and cause allergic irritations. Included in the term house dust are the fine particles produced in various fabrics of the house furnishings as well as those which enter into the fabrics. Some have advanced the theory that this house dust may be derived from microorganisms. The purpose of this new product is to immobilize the house dust. It can be applied to all fabrics which water does not harm. It is applied by sprinkling.

Known as Dust-Seal this new product has no odor. It creates no fire hazard in fabrics or on floors. It is nontoxic in concentrations employed, nonirritating and nonsensitizing. It is an oil compound which is so prepared that it mixes easily with water. By following directions the user can deposit an invisible transparent film on the major sources of allergenic dust in the environment, thereafter helping to keep the air clean. It is marketed by L. S. Green Associates.

Inositol

Deposits of cholesterol-protein macromolecules are responsible for arteriosclerosis or hardening of the arteries. Research has been carried on for many years in search of a cure for this condition. Now it has been reported by Ilka, Felch and Dotti that inositol, the muscle sugar, is capable of reducing the level of cholesterol in the blood. Experiments conducted on rabbits have revealed that animals fed both cholesterol and inositol showed a far smaller increase in cholesterol in the blood serum than did animals to which cholesterol alone was given. No results of tests on humans have been reported but it is believed that the same action should occur. In arteriosclerosis the body is no longer able to utilize food in the normal amount and in the normal way to provide energy so that the level of cholesterol in the blood rises. The cholesterol protein molecules are then deposited in small globules along the artery walls reducing the size of the passageway for the blood. As a consequence the heart is forced to work harder in circulating the blood, pressure rises and a cardiovascular incident is likely to occur. The lipotropic action of inositol is believed to retard this chain of events.

Ion Exchange Resins

In 1946 the possible therapeutic value of ion exchange resins in reducing edema was suggested but it was not until the American Chemical Society Meeting in September, 1950 that any definite results were reported. In congestive heart failure, cirrhosis of the liver and some types of hypertension the body retains salt causing an accumulation of excess body fluid, known as edema. The standard therapy in such conditions includes a low salt diet so as to prevent the formation of edema.

During World War II ion exchange resins were used to remove salt from sea water to make it potable. In the last year or so certain of these resins were made available for treating gastric ulcers. Now they have been found of value in relieving edema in the conditions mentioned above and there is no need for a salt-free diet. The ion exchange resins are defined as "insoluble materials which have the property of exchanging one chemical entity (an ion) for another. Where a specific ion is deleterious or objectionable in certain diseases or conditions, there is the possibility of using a resin to substitute other ions for the one objectionable."

A mixture of the potassium and ammonium forms has been used and it acts in the following manner: In the stomach and the upper intestinal tract, it gives off positively charged particles of potassium and ammonium. In exchange, it takes on hydrogen particles. Further down in the gastrointestinal tract the positive-charged hydrogen particles are released and the resin binds salt and potassium. The resin is not digested but is eliminated. It takes the salt from the body with it. The resins are given before meals and thus remove most of the sodium from the salted foods ingested.

Investigations of this usage for these resins is being conducted by Smith, Kline and French Laboratories and the Sterling-Winthrop Research Institute.

It is possible that the ion exchange theory also may be applied to therapy of virus infections since it has been found by Puck of the University of Colorado's Denver Medical Center, that a virus first attaches itself to a target cell because of an electrical attraction governed by charged metallic atoms, or ions, normally present in the cell's environment. The effect on the cell can be prevented by the introduction of metallic ions not present ordinarily. Ions, such as zinc, are capable of completely immunizing cells which are extremely

susceptible to invasion by a particular virus. It is hoped that further knowledge and understanding may lead to new methods of protection against invasion by different kinds of virus disease. It is possible that the ion exchange may even be accomplished after the virus has attacked the cell. However, if the virus has gone so far as to become an integral part of the cell the ion exchange is impossible. The second step in the virus attack, unfortunately, is irreversible.

King Snake Serum

The fact that the king snake is immune to the poisonous venoms of other snakes led to the investigation of the possible therapeutic value of its serum. Recently it was reported that a detoxicated serum from king snakes was capable of protecting mice from lethal doses of venom from water moccasins and rattlesnakes. Whether this observation will prove to have significance in the treatment of human beings has not yet been established. Further investigations are being conducted by Philpot and Smith of Tulane University and at the North Mississippi Hospital.

Kutrol

Uroenterone or anthelone is an extract of pregnancy urine which has been found effective in the treatment of crateriform duodenal ulcers. It does not inhibit gastric secretions when given orally. It is a buff-colored amorphous powder free from unpleasant odor or taste. The usual dosage is 150 mg. 4 times daily. With this dosage anthelone can be expected to induce remission of the ulcer within a period of three to six weeks. Adjunctive therapy, antispasmodics, sedatives, and alkalies with special dietary regimens may be required initially, although patients should be encouraged to maintain a normal three-meals-a-day schedule after reaching an asymptomatic stage. If relapse occurs therapy should be resumed. The longer the drug is administered the greater is the probability of prolonged remission.

The exact chemical nature of anthelone has not been determined but it is known that it does not contain any specific endocrine factors since they are removed in the processing. Parke, Davis and Co. have marketed anthelone under the tradename of Kutrol.

Mintacol

Diethyl-p-nitrophenyl phosphate is a synthetic found to be effective in glaucoma. It possesses 5 to 10 times the miotic power of physostigmine and acts more rapidly and more lastingly. It is being investigated by Bayer of Germany and is known as Mintacol.

Ompa

Octomethyl pyrophosphoramide is a slight variant of an insecticide used to kill various pests from rats to cockroaches. However, this particular variant known as Ompa has been found to be of value in medicine. Drs. Du Bois and Doull of the University of Chicago recently reported that Ompa relieves the symptoms of myasthenia gravis, the rare and incurable muscular disease. Ompa stimulates the nervous system and the muscles by inactivating cholinesterase and the result is the restoration of muscular strength.

Parvestin, Viodenum

For treating chronic ulcerative colitis there is being used a concentrated desiccated extract made from small intestine of pig. One heaping teaspoonful corresponds to about 4 oz. of fresh intestine. The product is known as Parvestin.

Viodenum also is being used for this condition. It contains whole desiccated and defatted duodenum which is believed to contain certain antisecretory and anti-proteolytic factors.

Poison Ivy Extract

Immunization or prophylaxis against poison ivy is another medical problem. Recently the use of a new extract has been reported. The extract has been tested on 113 patients, of these 77 per cent appeared to have satisfactory results after the first season of therapy. Eighty-four per cent had no poison ivy after therapy for 2 seasons and 92 per cent after 3 seasons. In the production of positive patch tests the new extract is just slightly less active than the usual alcoholic extract.

Larger and more rapidly increasing doses of the new extract may be given because it is more slowly absorbed. The extract is prepared by extraction of the toxic phenols from poison ivy leaves

with pyridine. The solution is then precipitated by adding aqueous alum with or without an aqueous mineral acid. Physically, the finished extract is a green flocculent precipitate suspended in normal saline. It is stable and causes no pain when injected.

A tuberculin syringe with a 26 gauge, ¼ inch needle can be used. Water is all that is necessary to cleanse the gauge and needle following use.

The course of injections recommended is as follows: 0.4 and 0.8 cc. of a 1:50 dilution, then 0.2, 0.6 and 1 cc. of a 1:5 dilution every 5 to 7 days, followed by 1 cc. of a 1.5 dilution monthly.

Pronestyl Hydrochloride

For the therapy of ventricular arrythmias a new drug was recently released. Chemically it is *p*-amino-N-(2-diethylaminoethyl) benzamide hydrochloride. It is also known as procaine amide hydrochloride and differs only by the presence of the amide grouping instead of the ester grouping in procaine.

Pronestyl hydrochloride has the empirical formula $C_{13}H_{21}N_3O.HCl$, with a molecular weight of 271.79.

Procaine amide hydrochloride is a white to tan crystalline powder. In the pure state, it melts at 167-8° C. It is soluble and fairly stable in acidified water but is insoluble in aqueous alkaline solutions. It is soluble in alcohol, slightly soluble in acetone, and insoluble in ligroin and benzene.

The action of this drug is believed to be due to a direct depressant action on the ventricular muscle. It has little effect on the auricles. Peripheral vasodilatation is partly responsible for the fall in blood pressure. No toxic effects have been observed following oral administration of this drug in doses of 3 to 6 Gm. daily for 2 days to 3 months. In some patients not having ventricular tachycardia intravenous administration of the drug produced a moderate and transient hypotensive effect. In those having ventricular tachycardia the hypotensive effect was striking in almost all cases. No hypotensive effects were reported when procaine amide hydrochloride was given to anesthetized patients.

This drug is indicated for the treatment of ventricular arrhythmias in conscious patients and for cardiac arrhythmias during anesthesia. The oral dosage is 0.25-0.5 Gm. every 4 to 6 hours as indicated. Intravenously the dosage is 0.2-1 Gm. When given during

anesthesia to correct ventricular arrhythmias the dosage is 100-500 mg. intravenously.

E. R. Squibb and Sons, Inc., are marketing this drug under the name, Pronestyl Hydrochloride.

Rabies Vaccine

An entirely new type of rabies vaccine for the prevention of canine rabies has been developed. The development of a strain of rabies virus, known as the Flury strain, was the starting point. This strain has never been passed through mammals but only through chicks and chick embryos. The virus has been attenuated by passage through chick brains and adapted to the chick embryo. This is a live modified virus vaccine, containing no mammalian nerve or other tissue. Its safety has been demonstrated by ample laboratory experimentations and through field trials on over 10,000 dogs. This vaccine gives longer-lasting protection than any other vaccine on the market. Studies show that one 3 cc. dose gives a more solid immunity at the end of one year than killed vaccines. While sufficient time has not yet passed to give definite data on the duration of protection, it is expected that it will protect for several years. The U. S. Bureau of Animal Industry has given approval for the sale of this vaccine under a special license but before it can be distributed state approval must be obtained. It is to be limited to use by veterinarians in dogs.

Known as Rabies Vaccine Modified Virus (Chick-Embryo Origin —Vacuum Dried) this product is being marketed by Lederle Laboratories Division, American Cyanamid Co.

Tryptar

Only about 50 per cent of patients with tuberculosis who develop purulent fluid in the chest recover. Those who have recovered have usually had to submit to radical, disfiguring surgery, which has not always been successful. A new type of therapy for this condition has been developed at Ohio State University College of Medicine. A solution of trypsin is used to wash out the chest daily for seven to ten days. The enzyme liquefies the pus and debris which can then be aspirated, thus cleansing the walls of the cavity in the chest. In a small series of cases, three persons were successfully treated with trypsin alone. In the remaining cases the chest cavities were sterilized and less radical surgery made possible. Only pure

crystalline trypsin can be used in the treatment. Further work is being done on this subject. Pure crystalline trypsin is supplied as Tryptar by Armour Laboratories.

Vasoxyl-P

For the convenience of physicians who wish to give the local anesthesia at the site of the lumbar puncture, and to make the intramuscular injection for pressor action, at the same time, as a single operation, a combination of methoxamine hydrochloride 15 mg. in 1 cc. procaine hydrochloride 1 per cent is now available. After injecting intradermally 0.1 to 0.2 cc. of the solution the needle is inserted deeply into the muscle tissue and the balance of the solution is injected. The amount of solution used for the intramuscular injection will depend on the dose desired, usually 10 to 15 mg. of methoxamine hydrochloride (0.7 to 1 cc. of solution). This solution is not intended for intrathecal administration nor is it to be used to produce spinal anesthesia. Under the tradename of Vasoxyl-P it is marketed by Burroughs Wellcome and Co., Inc.

Veriloid

The hypotensive ester alkaloids of *Veratrum viride* obtained by a special extraction process have recently been made available. This new process separates these active principles from inert material on a weight basis, less than one-tenth of one per cent of the crude drug from which it is derived. The finished product is standardized in dogs using blood pressure drop as the end point. Laboratory and clinical experience has shown that the results obtained in dogs are directly transferable to man, making for a product which is absolutely uniform in pharmacologic potency. This product is of value both in simple hypertension and in severe essential and malignant hypertension. Not only does it produce a sustained lowering of arterial tension through dilation of certain arterioles, but it also leads to gratifying relief of the subjective discomfort associated with hypertension. Drug tolerance is not developed. After the maintenance dose has been established, it may be given for months or years without decrease in clinical efficacy. Known as Veriloid this new form is marketed by Riker Laboratories, Inc.

SELECTED ABSTRACTS

Combined Effect of Penicillin and Sulfonamides on Gram Negative Organisms. El Borolossy, A. W. and Buttle, G. A. H. *J. Pharm. Pharmacol. 2:82* (1950). Since little had been reported on the synergistic effects of penicillin combined with sulfonamides the authors conducted a series of *in vitro* and *in vivo* tests on *Bacterium coli* and *Salmonella typhi.* The *in vitro* tests with *B. coli* were conducted using 0.1 mg. per cc. of sulfadiazine, sulfapyrazine, sulfathiazole, sulfamezathine, and sulfamerazine. These compounds were tested alone and in combination with various concentrations of penicillin ranging from 100 down to 1.56 units per cc. The least effective of the sulfonamides alone was sulfamerazine but none of them entirely prevented growth of the organism. Penicillin alone was also not very effective, 50 units per cc. being required to prevent all growth. However, the combination of any one of the sulfonamides with penicillin greatly augmented the effect. The tables given clearly show this effect. As an example, 6.25 units of penicillin per cc. did not suppress growth of the organism but when combined with any one of the sulfonamides there was complete suppression.

A synergism was evident from the results of *in vivo* tests also. Mice were injected with *B. coli* and at the same time were given the medication in a single dose. The effectiveness was evaluated on the basis of the prolongation of survival time of the infected mice above that of the controls. A comparatively large dose of 2000 units of penicillin only slightly prolonged the survival time of the mice. Each of the sulfonamides alone was more effective than the penicillin, giving an average survival time of 1.7 to 3.1 days as compared with 0.4 for the controls and 1.4 for penicillin alone. When the penicillin was combined with each one of the sulfonamides there was a marked synergistic effect. The best combination was with sulfamezathine when the average survival time increased from 1.7 days alone to 5.5 days with the combination. Along with the increased survival time went a better general condition of the animals.

In vitro experiments using *S. typhi* gave results similar to those obtained with *B. coli*. A concentration of 2.5 units of penicillin per cc. with 0.2 mg. of the sulfonamides per cc. prevented all growth. None of the agents alone prevented growth entirely but the sulfonamides were somewhat more effective than with *B. coli*. An even greater increase in the average survival time of mice was obtained with the combinations than was obtained on *B. coli*. The best effect was obtained with 2000 units of penicillin and 5 mg. of sulfamerazine with an increase in the average survival time from 0.7 days alone to 6.1 days combined with the penicillin.

The Use of Promacetin in the Treatment of Leprosy. Johansen, F. A., Erickson, P. T., Wolcott, R. R., Meyer, W. H., Gray, H. H., Prejean, B. M., and Sister Hilary Ross. *Pub. Health Rep. 65*:195 (1950). The need for a more rapidly acting remedy in the treatment of leprosy led to the trial of Promacetin (sodium 4,4′-diaminodiphenylsulfone-2-acetylsulfonamide). Although Promacetin is closely related chemically to Promin, Diasone, and Sulfetrone it is less toxic. Promacetin does not break down into diaminodiphenylsulfone and it is thought that this fact accounts for its lesser toxicity. Also, evidence has accumulated that even massive doses by mouth of Promacetin do not give dangerously high blood levels.

There were 26 lepromatous patients and 1 tuberculoid patient in the study group. Seventeen patients had received no previous treatment, 2 had received chaulmoogra oil, and 8 had received sulfones. Initially the dose of the drug was kept quite low, from 0.3 to 0.5 Gm. a day orally. The dosage was increased by increments of the initial dose every 2 weeks until a total of 3 to 4 Gm. a day were being administered. Careful clinical and laboratory examinations were conducted.

No severe acute toxic symptoms appeared in this group of patients. Minor complaints arose but none required suspension of treatment. A slight depression of the erythrocyte count may be expected during the first few weeks of treatment but unless there are other complications the count usually may be expected to return to normal spontaneously. However, studies involving larger groups

of patients are necessary before a definite statement can be made regarding the effect of this compound on the blood picture.

In general all 27 of these patients were improved at the end of their treatment periods. Those who had had no previous sulfone treatment showed objective improvement of a uniform, universal and sustained character, and subjective improvement manifested by an air of well being, increase in appetite and weight gain. Those who had previously had long periods of treatment with other sulfones benefited by a renewed clearing of skin lesions and by a further reduction of the number of leprosy bacilli in their specific lesions. Withdrawal of the drug caused a reappeaarnce of lesions in due time. The early improvement in the infected skin ulcerations suggested that Promacetin is capable of combating secondary infections as well as the leprosy bacilli. Skins smears commenced to show a noticeable reduction of bacilli at the end of one year of treatment while many patients showed an absence of bacilli in the mucous membranes at this time. The improvement obtained in the patients previously treated with other sulfones suggests that a wider application should be made of alternating treatment in leprosy, according to the authors.

Antigenic Activity of Dry BCG Vaccine. Birkhaug, K. *Am. J. Public Health 40:*545 (1950). The optimum antigenic activity of liquid BCG vaccine lasts but for a brief period of about 10 days. This makes necessary the distribution of the material for use in man before the vaccine can be properly controlled for purity, viable microorganisms, their tuberculogenic potency, and harmlessness. The need for a dry vaccine that would be stable for a long period of time is thus obvious.

A lyophilized BCG glucose vaccine was prepared and adjusted so that the original suspension contained 20 mg. of BCG suspension per cc. of 50 per cent glucose solution. The study revealed that the vaccine sustains a considerable loss of living elements during the lyophilization process. This apparently accounts for the fact that the dry vaccine has a lower antigenicity as demonstrated by the production of smaller skin lesions with graded doses of vaccine, a lower degree of tuberculin sensitivity, and a decreased resistance

against a challenge infection with virulent tubercle bacilli. Although there is a greatly reduced living population, the organisms surviving retained their original cultural, morphological, and biological characteristics.

The author reported that parallel studies were in progress using the same living population of BCG in fresh liquid vaccine as in a dry vaccine in order to try to prove the belief that the difference between the two types of vaccines is quantitative rather than qualitative. If this is the case it would seem probable that identical antigenic reactions could be obtained by adjusting the dosage of living elements in the resuspended dry vaccine to correspond to the dosage in the fresh vaccine. The usual dosage, intracutaneously, of 0.05 to 0.1 mg. of BCG contains 1,750,000 to 3,500,000 living elements. Such a dose is capable of producing a tuberculin positive reaction in almost 95 per cent of vaccinated children and adults within a period of about 8 weeks. Although some of these positive reactors may become tuberculin negative a year or so later the average duration of the allergy produced by one single inoculation of BCG is in the neighborhood of 5 years. If the dry vaccine was adjusted to a dosage corresponding to that of the fresh liquid vaccine there would be present a large proportion of killed elements which would increase the allergenic impact of the vaccine.

The dry vaccine was demonstrated to maintain its viability for a period of more than one year when stored at 2° C. to 4° C. This advantage makes possible the carrying out of desirable tests for its purity, harmlessness, and antigenic potency before it is released for use in human beings. Such a product would also make the vaccine available for use in localities not having access to fresh liquid vaccines. Studies are in progress to try to determine a method for preparing the dry vaccine so that all of the antigenic constituents of the fresh vaccine will be retained.

Considerations on the Mechanism of Cure of Bacterial Endocarditis. Hunter, T. H. *J. A. M. A. 144*:524 (1950). Subacute bacterial endocarditis can usually be cured by a prolonged and intensive treatment with penicillin. However, a certain number of cases, particularly those having enterococci present in the vegeta-

tions, prove to be refractory to usual treatment. Also, the usual 4 to 8 week course of treatment is costly and inconvenient. Therefore, the author considered several of the antibiotics, singly and in combinations, and their possible role in the control of this disease.

The author pointed out that clinical evidence has shown that the host practically never eradicates this infection alone. Therefore, bacteriostasis could not be expected to provide a final cure. The antibiotic or combination should be bactericidal.

In vitro studies were performed on the enterococcus *Streptococcus liquefaciens*, strain L. W. It was found that inhibition tests showed aureomycin was much more effective than chloramphenicol, penicillin or streptomycin, and that the effect of penicillin and aureomycin was additive but that of penicillin and streptomycin was not. The author emphasized that these tests merely measure bacteriostasis. It is his belief that because such tests do not measure the bactericidal effect the results are often misleading. To further study this aspect the killing effect on the bacteria under various conditions was tested. It was found consistently that combinations of penicillin and aureomycin were unable to produce a complete kill in a culture but that penicillin and streptomycin in combination completely sterilized the culture. Streptomycin alone had practically no effect. Penicillin alone greatly reduced the number of bacteria but did not sterilize the culture.

The results of this study led the author to treat 3 patients with a single 10 day course of penicillin and streptomycin in combination. He reported that all 3 were doing well one month after cessation of treatment. *In vitro* studies coupled with clinical experience must be the means of evaluation of the treatment of this disease for the bacteria usually encountered are not pathogenic to laboratory animals.

Hexamethonium Bromide in the Treatment of Severe Hypertension. Campbell, A. and Robertson, E. *Brit. Med. J. No. 4683*:804 (1950). Although the place of hexamethonium bromide in the treatment of severe hypertension has not yet been definitely established this preliminary report was presented because this compound seems to provide a useful method of reducing the blood pressure in severe cases of hypertension, with relatively low toxicity.

The authors found that a more constant fall of the blood pressure was obtained when the drug was taken orally than when it was given in doses of 100 mg. intramuscularly. Therefore, the oral route was followed with an initial dose of 0.25 Gm. in about 10 cc. of water. This dose was given twice on the first day. On the next 2 days this dose was given 3 times daily and then 0.5 Gm. was given 3 times a day for 2 days. Similar increments were given until 0.5 Gm. was given 4 to 6 times a day by the tenth day. This daily dose of 2 to 3 Gm., preferably given before meals, was found to maintain a blood level decreased to normal or to what was felt to be an optimum level.

Eight cases of hypertension with papilloedema were cited by the authors. Headache was abolished, papilloedema was markedly reduced, and vision was improved in every case. Paroysmal nocturnal dyspnoea was completely relieved in 3 cases and angina in one case. There was practically no alteration of the balance of fluid intake and output during treatment. Treatment was withdrawn from 3 patients without an immediate rise in blood pressure. One of the 3 had maintained a normal pressure level after 8 weeks.

The side effects of blurring of vision, dry mouth, nausea, heartburn, and constipation were encountered in every patient from the beginning of treatment. However, these side effects were not severe and had disappeared within 2 weeks, but they did recur and disappear with any significant increase in dosage. An initial large dose brought about a circulatory collapse in 2 patients but an initial small dose with increments as described circumvented this difficulty. Substitution of pentamethonium bromide and iodide in a few instances indicated that this drug was less effective than hexamethonium bromide.

A Study of the Effectiveness of Avianized Anti-Rabies Vaccine. Starr, L. E., Stafford, A. L. and Dye, O. B. Proc. Fifty-Third Ann. Meet. U. S. Livestock and Sanitary Assoc. All species of warm blooded animals are susceptible to rabies. Since the disease is transmitted almost entirely by tooth wounds inflicted by rabid animals transmission is limited largely to canine and feline animals. The dog is the most important animal in the transmission of the disease but epidemics occasionally occur among foxes, wolves and other wild animals.

The field trial of the avianized chick embryo vaccine involved 422 dogs, 121 cattle, and 15 goats. The vaccine contained living rabies virus of the Flury strain which had been fixed by successive chick embryo passage. Such a living virus could be expected to produce a long lasting immunity and, since it contained little brain tissue it should not produce the reactions and paralysis which occasionally follow the injection of brain tissue, as in the usual rabies vaccine. All of the dogs in the study had remained normal with no cases of rabies and no deaths attributable to the vaccine, although 5 dogs met accidental deaths. No abscesses occurred at the site of injection. Sixteen of the cattle died of a Street rabies virus apparently inflicted before vaccination. The authors pointed out that no rabies vaccine yet known will give protection in less than about 30 days. However, no Flury strain virus was recovered from any of the animals. All of the goats remained normal except 2 which died because of screw-worm injury.

The authors concluded that injection of the vaccine will not cause rabies in dogs, cattle, or goats. It will not produce abscesses at the site of injection nor paralysis or other reactions. There is no reaction when it is used on previously immunized animals. Further study is necessary in order to determine the proper dosage, the minimum time necessary to produce an immunity, and the duration of that immunity in domestic animals.

Folic Acid and Vitamin B_{12} Therapy in Anemia. Spies, T. D., Lopez, G. G., Milanes, F., Toca, R. L., and Rebordeo, A. *GP 2:37* (1950). Evidence has accumulated that both vitamin B_{12} and folic acid have specific hemopoietic and clinical functions in the treatment of certain anemias. However, in the majority of cases both of these substances are effective hemopoietically and each has an additive effect when administered along with the other. The specific function of vitamin B_{12} not possessed by folic acid is evident in the treatment of acute neurological manifestations often associated with pernicious anemia and occasionally with tropical sprue. On the other hand the authors have found that certain cases of megaloblastic anemia, particularly the pernicious anemia of pregnancy and the megaloblastic anemia of infancy, are refractory to vitamin B_{12} or to highly refined liver extract preparations but respond to folic acid.

The authors pointed out that anemia is a symptom and nothing more, and that thorough clinical, laboratory and dietary studies are essential in order to properly classify this disease. Even then satisfactory classification is not always possible. In many situations satisfactory etiologic diagnostic evidence and clinical information is not available to make a satisfactory diagnosis and classification of the anemia condition. In such cases the authors advised that there should be no hesitancy in employing both vitamin B_{12} and folic acid together in treatment. Both of these substances occur naturally in liver and are nontoxic. It would seem to stand to reason that both of these substances have specific functions as well as functions in common, and both are necessary.

The response of individuals varies widely with dosage of these substances. However, the usual dosage employed by the authors was 10 milligrams of folic acid orally a day and 150 micrograms of vitamin B_{12} orally or 25 micrograms intramuscularly a day either alone or in combined therapy. Adequate therapy usually brought about a prompt hemopoietic and clinical response. One case used to illustrate the effect of combined therapy was that of a woman in relapse with the macrocytic anemia of pregnancy. She was too weak to sit up in bed and had an initial blood picture of: red blood cells, 2.41 million; hemoglobin, 10.0 Gm. (65 per cent); and reticulocytes, 1.4 per cent. There was only a slight improvement in the blood picture and no improvement in the clinical condition after 30 days of oral and intramuscular vitamin B_{12} therapy. She was then given 150 micrograms of vitamin B_{12} and 10 milligrams of folic acid a day orally. On the fourth day she suddenly regained her appetite and volunteered that she felt stronger than she had felt for weeks. By the tenth day the reticulocytes had increased to 20 per cent and there was an increase of 700,000 red blood cells and 1.5 Gm. of hemoglobin. The next day she was allowed to return home, feeling well. This gain was maintained with a normal peripheral blood picture and normal bone marrow from a sternal puncture six weeks after discharge from the hospital. During the interim she had been given 5 mg. of folic acid orally a day.

The authors concluded that the physician who makes every effort to arrive at a precise diagnosis and applies persistent and adequate therapy with these substances will obtain a gratifying clinical and hemopoietic response.

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